Full Text DK-92-20

HORMONAL REGULATION OF BONE IN HEALTH AND DISEASE

NIH GUIDE, Volume 21, Number 22, June 12, 1992

RFA: DK-92-20

P.T. 34

Keywords:
Musculoskeletal System
Hormones
PHYSIOLOGICAL/DEVELOPMENT PROCESS

National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: July 10, 1992
Application receipt Date: August 25, 1992

PURPOSE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invite investigator-initiated research grant applications to elucidate the role(s) of systemic and local hormones, growth factors, and cytokines on bone in health and disease.

HEALTHY PEOPLE 2000

The PHS is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the

Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Minority individuals and women are encouraged to submit as Principal Investigators.

MECHANISM OF SUPPORT

Support of this program will be through the NIH research project grant (R01) award. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Except as otherwise stated in this announcement, awards will be administered under PHS grants policy as stated in the PHS Grants Policy Statement.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to the customary peer review procedures. The total requested project period for applications submitted in response to this RFA may not exceed five years. A maximum of three years may be requested for foreign awards.

FUNDS AVAILABLE

For FY 1993, $2,000,000 will be committed by the NIDDK to fund applications submitted in response to this RFA and an additional $2,000,000 will be committed by the NIAMS. However, this funding level is dependent upon the receipt of a sufficient number of applications of high scientific merit. In order to help meet NIH goals for managing the costs of biomedical research, applicants must limit requests to not more than $160,000 direct costs for the initial budget period. Although this program is provided for in the financial plans of the NIDDK and the NIAMS, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

RESEARCH OBJECTIVES

Background

Bone disease, particularly osteoporosis, is a major health problem, prevalent primarily in women, that adversely affects large segments of the population. Approximately 1.5 million fractures occur each year in the United States that may be attributable to osteoporosis, with major and significant socioeconomic impact. It is estimated that there is a lifetime risk of hip fracture of 15-30 percent for women and 5-10 percent for men. In 1986, the annual cost of osteoporosis was estimated in the range of $7 to 10 billion. Therefore, osteoporosis accounts for a large component of health-care costs and human suffering with attendant individual pain and loss of productivity. Other bone disorders, such as Paget's disease, renal osteodystrophy, and hyperparathyroidism, also cause significant morbidity. Many of the causes and potential treatments for bone disease have a basis in the endocrinology of bone cell physiology.

Alterations in hormone production and/or action are major contributing factors to osteoporosis and other disorders of bone. Although many clinical studies and trials have focused on understanding the pathophysiology and potential pharmacologic therapeutics involved in osteoporosis and other bone disorders, knowledge of basic concepts of the hormonal regulation of bone cell development, structure, and function is inadequate. Specifically, questions pertaining to the roles of systemic hormones versus locally active growth factors and/or cytokines on the cells that regulate bone mass need to be answered. At the molecular level, many of the effects of hormonal actions are reflected in specific changes in gene expression. The nature and mechanisms of these changes in response to steroid and/or peptide hormones requires definition. The purpose of this solicitation is to stimulate investigation of the role of systemic and local hormones and other endocrine factors in bone physiology and pathobiology. The results of this research should enhance understanding of the hormonal regulation of bone, contribute to the knowledge of the pathogenesis of osteoporosis and other bone disorders, and ultimately lead to new strategies for prevention and treatment of these disorders.

Scope

Some examples of research topics that would be considered responsive to this solicitation include the following:

o basic studies on the molecular and cellular action of estrogen, other sex steroids, antiestrogens, 1,25(OH)2 D3, glucocorticoids, retinoic acid, T3 and other members of the steroid/thyroid hormone superfamily, and the analogues, on bone;

o the effects of interactions between systemic hormones (e.g., PTH/PTHrP, calcitonin (CT), estrogen, thyroid hormone, Growth Hormone) and local factors (e.g., IGF-I, cytokines) on bone;

o the roles of local growth factors and/or cytokines and lymphokines on the endocrine/paracrine/autocrine regulation in effecting hormonal action on bone in health and disease;

o studies of the mechanism of action by which CT and PTH/PTHrP act through the novel G-protein subfamily of receptors in effecting physiological regulation at the level of bone and other cells;

o identification of the target genes for bone-active hormones/growth factors/cytokines and elucidation of the regulatory elements involved;

o mechanisms of hormonal signal transduction in bone cells, identification of the type(s) of response that take place, and whether or not different pathways mediate the responses to hormones with the same end result

These areas of interest are not listed in any order or priority. They are only suggested examples of areas of research. Applicants are encouraged to propose other areas that are related to the objectives and scope described above.

SPECIAL REQUIREMENTS

Interdisciplinary approaches may be needed for these studies with expertise required in one or more of the following areas: molecular and cellular biology, endocrinology, physiology, pathology, and pharmacology.

SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants/offerors are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of Unites States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventative strategies), diagnosis, or treatment or diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

LETTER OF INTENT

Prospective applicants are asked to submit, by July 10, 1992, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application is being submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is helpful in planning for the review of applications. It allows NIDDK staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent is to be sent to:

Chief, Review Branch
Division of Extramural Activities
National Institute of Diabetes and Digestive and Kidney Diseases
Westwood Building, Room 605
5333 Westbard Avenue
Bethesda, MD 20892
Telephone: (301) 496-7083

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. The form is available from most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/496-7441.

The RFA label available in the PHS 398 application form must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and check the YES box.

Submit a signed, typewritten original of the application, including the Checklist, and four signed, exact photocopies, in one package to:

DIVISION OF RESEARCH GRANTS
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

At time of submission, two additional copies of the application must also be sent under separate cover to:

Chief, Review Branch
Division of Extramural Activities
National Institute of Diabetes and Digestive and Kidney Diseases
Westwood Building, Room 605
5333 Westbard Avenue
Bethesda, MD 20892

Applications must be received by August 25, 1992. If an application is received after that date, it will be returned to the applicant. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. However, it is allowable to submit the same project as both an R01 and as a component project of a program project. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications previously reviewed. Such applications must not only include an introduction addressing the previous critique but also be responsive to this RFA.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the program requirements and criteria stated in the RFA is an NIDDK staff function. If the application is not responsive to the RFA, NIDDK staff will contact the applicant to determine whether it should be returned to the applicant or held until the next receipt date and reviewed in competition with all other unsolicited applications.

Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific/technical merit by an appropriate peer review group convened by the NIDDK. Applications may be subjected to triage by an NIDDK peer review group to determine scientific merit relative to other applications received in response to this RFA. If the number of applications submitted is large compared to the number of awards to be made, a preliminary scientific peer review may be conducted and applications withdrawn from further competition if not competitive for the award. The NIDDK will notify the applicant and institutional official of this action.

Those applications judged to be competitive will be reviewed for scientific and technical merit in accordance with the usual NIH peer review procedures by an initial review group specifically convened for this RFA. Following this review, the applications will be given a secondary review by the NIDDK and NIAMS Advisory Councils unless not recommended for further consideration by the initial review group.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications.

o scientific/technical merit criteria specific to the objectives of the RFA;

o scientific, technical, or medical significance and originality of proposed research;

o appropriateness and adequacy of the experimental approach and ethodology proposed to carry out the research;

o qualifications and research experience of the Principal Investigator and staff, particularly, but not exclusively, in the area of the proposed research;

o availability of resources necessary to perform the research;

o appropriateness of the proposed budget and duration in relation to the proposed research; and

o if an application involves activities that could have an adverse effect upon humans, animals, or the environment, the adequacy of the proposed means for protecting against or minimizing such effects.

The following additional criterion applies to applications from foreign institutions:

o uniqueness of research such that it can only be performed outside of the United States.

Schedule

Letter of Intent Receipt Date: July 10, 1992
Application Receipt Date: August 25, 1992
Initial Review: October/November 1992
Second Level Review: January/February 1993
Anticipated Award: April 1, 1993

AWARD CRITERIA

Applications will compete for available funds with all other applications responsive to this RFA. The following will be considered in making funding decisions:

o Quality of the proposed project as determined by peer review

o Availability of funds

o Program balance among the research areas represented in this RFA.

The anticipated date of award is April 1, 1993.

INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged.

Direct inquiries regarding programmatic issues should be directed to:

Ronald N. Margolis, Ph.D.
Director, Endocrinology Research Program
Division of Diabetes, Endocrinology and Metabolic Diseases
National Institute of Diabetes and Digestive and Kidney Diseases
Westwood Building, Room 621
Bethesda, MD 20892
Telephone: (301) 496-7504

Joan A. McGowan, Ph.D.
Chief, Bone Biology and Bone Diseases Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 403
Bethesda, MD 20892
Telephone: (301) 480-7881

Direct inquiries regarding fiscal matters should be directed to:

Sharon Tempchin
Grants Management Specialist, DEA
National Institute of Diabetes and Digestive and Kidney Diseases
Westwood Building, Room 649
Bethesda, MD 20892
Telephone: (301) 496-7467

Carol Clearfield
Grants Management Specialist
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 403
Bethesda, MD 20892
Telephone: (301) 496-7495

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance sections 93.847 and 93.846. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulation 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

Return to RFAs Index
Return to NIH Guide Main Index